Respiratory Medicine (2007) **101**, 326–332

ELSEVIER

respiratoryMEDICINE

Comprehensive pulmonary rehabilitation according to severity of COPD

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Received 30 August 2005; accepted 28 March 2006

KEYWORDS
Pulmonary rehabilitation;
COPD;
Classification of severity;
Pulmonary function;
6-min walk test

Summary A new classification for the severity of COPD was proposed at GOLD 2003: stage I: $FEV_1 \geqslant 80\%$ predicted; stage II: $50\% \leqslant FEV_1 < 80\%$; stage III: $30\% \leqslant FEV_1 < 50\%$; and stage IV: $FEV_1 < 30\%$. To elucidate the acute effects of pulmonary rehabilitation (PR) on patients with different stages of COPD, data on pulmonary function, arterial blood gas analysis, the 6-min walk test, respiratory muscle strength, and activities of daily living were analyzed before and after our comprehensive 4- to 8-week inpatient PR program between 1992 and 2003. A total of 225 patients (201 men and 24 women; 21 with stage II, 79 with stage III, and 125 with stage IV COPD) was assessed. There were significant differences in FEV_1% predicted and % residual volume in stages III and IV, in % vital capacity in stages II, III and IV, and in % total lung capacity in stage II when comparing the changes between pre- and post-PR. Significant differences of PaO_2 in stages III and IV and $PaCO_2$ in stage IV were found when comparing the changes between pre- and post-PR. The 6-min walk distance was significantly increased after PR by an average of approximately 50 m for all staged patients. Respiratory muscle strength was also significantly increased in stages III and IV. Activities of daily living were significantly improved in all stages. These results showed that patients with COPD had benefited

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0954-6111/$ - see front matter
doi:10.1016/j.rmed.2006.03.044

from PR regardless of disease severity. The effects included improvement in pulmonary function, arterial blood gas analysis, 6-min walk distance, respiratory muscle strength, and activities of daily living although there were some differences among the three stages.

Introduction

Pulmonary rehabilitation (PR) is an effective intervention in patients with COPD.[1,2] Berry et al.[3] reported that all patients with COPD benefited from PR, regardless of the severity of the disease. They defined disease severity according to the 1995 American Thoracic Society (ATS) scale.[4] Using the 1-s forced expiratory volume (FEV_1), severity was classified into three stages: stage I: $FEV_1 \geqslant 50\%$ predicted; stage II: $35\% \leqslant FEV_1 < 50\%$; and stage III: $FEV_1 < 35\%$. A new classification of severity was proposed in the GOLD 2003 guideline.[5] The new guideline defines 5 stages: stage 0: normal spirometry with chronic symptoms; stage I: $FEV_1 \geqslant 80\%$ predicted; stage II: $50\% \leqslant FEV_1 < 80\%$; stage III: $30\% \leqslant FEV_1 < 50\%$; and stage IV: $FEV_1 < 30\%$. Stages I, II and III of the 1995 ATS classification approximately correspond to stages II, III, and IV of the GOLD 2003 classification, respectively, in terms of the values of FEV_1 predicted.[2] PR was recommended from stage II ($FEV_1 < 80\%$) COPD patients.[5] To the best of our knowledge, there have been no reports that describe the effect of comprehensive PR on COPD on the basis of the new staging. To elucidate the benefit of PR for patients with new stages II, III, and IV COPD, we analyzed data on pulmonary function, arterial blood gas analysis, the 6-min walk test, respiratory muscle strength, and activities of daily living (ADL) before and after our inpatient PR program.

Methods

The diagnosis of COPD and the classification of severity were defined according to the global strategy for the diagnosis, management, and prevention of COPD updated in 2004.[6] The patients had symptoms of cough, sputum, or dyspnea, and/or a history of exposure to risk factors for the disease. The presence of a post-bronchodilator $FEV_1 < 80\%$ of the predicted value in combination with an FEV_1/forced vital capacity (FVC) $< 70\%$ confirms the presence of airflow limitation that is not fully reversible. Reversibility was defined as an increase in FEV_1 greater than 12% and/or 200 mL after inhalation of β-agonist. The classification of severity was as follows: moderate COPD (stage II), $50\% \leqslant FEV_1 < 80\%$ predicted; severe COPD (stage III), $30\% \leqslant FEV_1 < 50\%$; and very severe COPD (stage IV), $FEV_1 < 30\%$. The inclusion criteria for this study were: (1) stage II, III or IV COPD, (2) the ability to walk for 6 min, (3) never having participated in a rehabilitation program before, and (4) the absence of a comorbid disease that would preclude the patient from participating in a rehabilitation program. The patients received optimal medical treatment including β-agonists, anticholinergic drugs, theophylline, and/or (inhaled or oral) steroids. A stable condition whilst receiving medical treatment was required before PR commenced.

Baseline data recorded before PR consisted of height, body weight, body mass index (BMI), serum total protein and albumin levels, smoking status, and the use of supplemental oxygen at home. Pulmonary function data such as FEV_1, FEV_1% predicted, FEV_1/FVC, vital capacity (VC), %VC, % total lung capacity (TLC), and % residual volume (RV) were assessed by spirometry and lung volume testing with helium dilution (Chestac-25, Chest, Tokyo, Japan). Predicted FEV_1 values were obtained from the Japanese Respiratory Society guideline[7]: FEV_1 (L) for men $= 0.036 \times$ height (cm) $- 0.028 \times$ age (yr) $- 1.178$; FEV_1 (L) for women $= 0.022 \times$ height (cm) $- 0.022 \times$ age (yr) $- 0.055$. Arterial blood gases were taken at rest. Patients with hypoxemia at rest (< 55 Torr) were prescribed oxygen therapy, meaning that PaO_2 and $PaCO_2$ were measured while they were receiving oxygen. The maximal inspiratory (PI_{max}) and expiratory (PE_{max}) mouth pressures were measured using a respiratory muscle dynamometer (Vital power KH-101 Chest, Tokyo, Japan). The patients performed 6-min walk (6 MW) tests. The 6-min walk distance (6 MWD) was defined as the longest distance possible without encouragement. Subjects were allowed to stop and rest if necessary. The first 6 MWD without a training session was accepted. The subjects walked with hemoglobin oxygen saturation (SpO_2) monitors. ΔSpO_2 (SpO_2 level just before 6 MW—minimum SpO_2 level during 6 MW) was also assessed. ADL was assessed using questionnaires based on velocity of motion and shortness of breath in daily activity with various grades

(0, 1, 2, or 3) of exertion including eating, defecation, face washing, brushing teeth, bathing, dressing, walking in a room, walking in wards, walking in the hospital, walking up the stairs, and shopping (Table 1).[8,9] A perfect score of the two parameters is 30 points each and higher scores mean greater daily activity. These baseline measurements were made during the week before and after PR.

Comprehensive PR was performed using a 4- to 8-week hospital-based program. Patients attended the rehabilitation unit on 5 half-days per week. Exercise included cycle ergometer training (5 min), treadmill training (5 min), upper and lower extremity strength training (5–10 min), breathing therapies (5–20 min), and relaxation therapies (10–20 min) for total 30–60 min. Patients underwent both cycle ergometer and treadmill training. The exercise strength of the training was based on tolerance determined by symptomatic and physiologic criteria resulting from exercise tests. Pulse oximetry was used to supervise patients during exercise. If the SpO_2 fell below 90%, oxygen supplementation was provided to maintain an $SpO_2 \geqslant 90\%$. During exercise, the target pulse rate was determined by the formula: (138—Age $\times$ 0.5).[10] If the patients or physical therapists considered the workload to be low or if the patients did not reach their target pulse rate, the physical therapists increased workload by steps of 25% until the workload was appropriate or until the target pulse rate was reached. If patients could not tolerate the workload because of dyspnea or leg fatigue, or if the pulse rate was more than 10/min above the target pulse rate, the physical therapists allowed the patient to rest and decreased the workload by 25%.

Table 1 Assessment of ADL.

	Velocity of motion	Shortness of breath
Eating	0, 1, 2, or 3	0, 1, 2, or 3
Defecation	0, 1, 2, or 3	0, 1, 2, or 3
Face washing and brushing teeth	0, 1, 2, or 3	0, 1, 2, or 3
Bathing	0, 1, 2, or 3	0, 1, 2, or 3
Dressing	0, 1, 2, or 3	0, 1, 2, or 3
Walking in a room	0, 1, 2, or 3	0, 1, 2, or 3
Walking in wards	0, 1, 2, or 3	0, 1, 2, or 3
Walking in the hospital	0, 1, 2, or 3	0, 1, 2, or 3
Walking up the stairs	0, 1, 2, or 3	0, 1, 2, or 3
Shopping	0, 1, 2, or 3	0, 1, 2, or 3
Total	/30	/30

Scores for velocity of motion are 0: impossible or almost impossible; 1: impossible without rest; 2: possible but slow; 3: possible with ease. Scores of shortness of breath are 0: intolerable; 1: hard; 2: easy; 3: no shortness of breath.

Educational activities included an understanding of pulmonary pathophysiology, the mechanisms of breathlessness, the importance of exercise and nutritional support, pulmonary medications, how to deal with breathlessness and exacerbations, how to clear sputum, how to apply the lessons of rehabilitation to daily life, the usefulness of oxygen therapy, the indications for lung volume reduction surgery (LVRS), and the importance of smoking cessation. Twelve educational sessions per month were delivered by seven doctors, three specialist respiratory nurses, a physical therapist and a dietician, and educational videos were shown instead of lectures on the other days. This education program was 30 min long on weekdays and was repeated every month.

Statistical analyses were performed using the SPSS Base System™ and Advanced Statistics™ programs (SPSS, Chicago, IL, USA). To compare categorized variables between different stage groups, the Mann-Whitney *U* test was used. Nonparametric paired variables between before and after PR were analyzed with the Wilcoxon test.

Results

Between July 1992 and June 2003, 201 men and 24 women who participated in our PR program (for a median period of 5 weeks) were assessed in this study. The patient characteristics of the 225 patients (21 at stage II, 79 at stage III, and 125 at stage IV) are shown in Table 2. The median age of all the patients was 69 yr (range 45–84 yr). The younger patients were categorized in the more severe stages and there were significant differences in ages between each stage ($P = 0.028$ for stage II and III, $P = 0.002$ for stage III and IV). Measures of nutritional status such as BMI, total protein and albumin levels, and smoking index were not significantly different among the three groups. Home oxygen therapy was administrated to patients with more advanced COPD.

Pulmonary function data on pre-PR and post-PR by stage are shown in Table 3. Before PR, FEV_1, FEV_1% predicted, FEV_1/FVC, and %VC were decreased to a greater extent in the more advanced stages: all *P* values are 0.000 between stage II and III or between stage III and IV. The difference in VC between stage II and III was not significant ($P = 0.083$), but was significant ($P = 0.000$) between stage III and IV. Although there were no differences in %TLC among the three stages, %RV

Table 2 Patient characteristics.

	Stages		
	II ($n = 21$)	III ($n = 79$)	IV ($n = 125$)
Sex (men/women)	15/6	68/11	118/7
Age (median yr, range)	72 (63–81)	69 (54–84)	67 (45–79)
Height (cm)	158.3 ± 7.5	160.6 ± 6.4	162.3 ± 6.6
Weight (kg)	48.2 ± 9.0	50.1 ± 9.3	48.8 ± 9.1
Body mass index (kg/m^2)	19.1 ± 2.6	19.3 ± 3.1	18.5 ± 3.2
Total protein (g/dL)	6.8 ± 0.6	6.7 ± 0.6	6.5 ± 0.5
Albumin (g/dL)	3.8 ± 0.4	3.9 ± 0.4	3.9 ± 0.4
Smoker/never-smoker	21/0	77/2	121/4
Smoking index	1019 ± 499	1102 ± 667	1160 ± 675
Oxygen therapy (yes/no)	3/18	25/54	75/50

Values for height, weight, total protein, albumin, and smoking index (= cigarettes/day × year) are means ± standard deviation.

Table 3 Pulmonary function data: pre- and post-pulmonary rehabilitation (PR) by stage.

Parameters	Stages		
	II	III	IV
FEV_1 (L)			
Pre-PR	1.40 ± 0.30	0.97 ± 0.23	0.63 ± 0.13
Post-PR	1.43 ± 0.32	1.06 ± 0.36	0.75 ± 0.21
P	0.268	0.015	0.000
FEV_1 (% predicted)			
Pre-PR	60.2 ± 7.0	37.5 ± 6.2	22.7 ± 4.5
Post-PR	62.0 ± 9.2	40.4 ± 11.3	27.1 ± 7.3
P	0.212	0.014	0.000
FEV_1/FVC (%)			
Pre-PR	55.8 ± 8.6	45.7 ± 8.6	39.8 ± 9.6
Post-PR	52.9 ± 6.6	47.0 ± 11.7	39.1 ± 9.7
P	0.126	0.470	0.159
VC (L)			
Pre-PR	2.80 ± 0.67	2.51 ± 0.64	1.98 ± 0.58
Post-PR	2.97 ± 0.70	2.69 ± 0.72	2.27 ± 0.58
P	0.009	0.010	0.000
%VC (%)			
Pre-PR	96.0 ± 14.7	80.5 ± 15.4	61.0 ± 16.6
Post-PR	103.4 ± 17.6	85.6 ± 18.3	69.9 ± 16.1
P	0.019	0.012	0.000
%TLC (%)			
Pre-PR	127.8 ± 11.2	138.8 ± 39.7	137.6 ± 76.3
Post-PR	133.1 ± 15.1	127.1 ± 20.3	128.9 ± 21.3
P	0.123	0.023	0.565
%RV (%)			
Pre-PR	197.7 ± 34.0	246.1 ± 122.5	265.9 ± 127.8
Post-PR	194.4 ± 35.0	199.3 ± 64.3	214.4 ± 52.6
P	0.575	0.003	0.003

Values are means ± standard deviation.

increased from stages II to IV ($P = 0.008$). There were significant differences of FEV_1, FEV_1% predicted and %RV in stages III and IV, VC and %VC in three stages, and of %TLC in stage II when comparing the changes between pre- and post-PR. Arterial blood gas data are shown in Table 4. Significant differences in pH were found among the three stages before PR (stage II versus stage III: $P = 0.010$; stage III versus stage IV: $P = 0.000$). Although there were no differences in PaO_2 among three stages, $PaCO_2$ was elevated in patients with more advanced stage before PR (stage II versus stage III: $P = 0.000$; stage III versus stage IV: $P = 0.000$). Significant differences of PaO_2 in stages III and IV and $PaCO_2$ in stage IV and were found when comparing the changes between pre- and post-PR. The results of the 6 MW test are shown in Table 5. Although there were no differences in distance or ΔSpO_2 between stages II and III, there were significant differences between stages III and IV before PR (distance: $P = 0.000$; ΔSpO_2: $P = 0.003$). 6 MWD in three stages was significantly increased after PR up to approximately 50 m. ΔSpO_2 was significantly increased (by an average of 1.4%) in patients with stage IV. There were no differences in respiratory muscle strength such as PE_{max} and PI_{max} in the three stages before PR and respiratory muscle strength was significantly improved in stages III and IV (Table 6). There was no difference in ADL between stages II and III, but a significant difference between stages III and IV before PR (velocity of motion: $P = 0.000$; shortness of breath: $P = 0.000$). The scores of both parameters improved significantly after PR in all stages (Table 7).

Discussion

PR is an effective treatment for patients with COPD in terms of exercise capacity and health-related

Table 4 Arterial blood gas data: pre- and post-pulmonary rehabilitation (PR) by stage.

Parameters	Stages		
	II	III	IV
pH			
Pre-PR	7.45±0.04	7.43±0.03	7.41±0.03
Post-PR	7.43±0.02	7.43±0.03	7.41±0.03
P	0.083	0.719	0.158
PaO_2 (Torr)			
Pre-PR	71.1±5.9	68.8±9.3	68.3±10.9
Post-PR	72.1±9.6	71.6±9.4	70.6±10.1
P	0.881	0.013	0.008
$PaCO_2$ (Torr)			
Pre-PR	36.4±3.4	40.4±4.9	47.3±8.6
Post-PR	37.4±3.9	40.0±4.4	45.7±7.0
P	0.204	0.461	0.014

Values are means±standard deviation.

Table 5 The 6-min walking test: pre- and post-pulmonary rehabilitation (PR) by stage.

Parameters	Stages		
	II	III	IV
Distance (m)			
Pre-PR	340±84	341±81	289±95
Post-PR	388±59	388±78	341±79
P	0.015	0.000	0.000
ΔSpO_2 (%)			
Pre-PR	6.9±6.9	6.0±4.6	8.2±5.5
Post-PR	5.0±3.4	7.0±4.5	9.6±5.6
P	0.819	0.100	0.007

Values are means±standard deviation.

Table 6 Respiratory muscle strength: pre- and post-pulmonary rehabilitation (PR) by stage.

Parameters	Stages		
	II	III	IV
PE_{max} (cmH_2O)			
Pre-PR	48.3±19.0	55.8±21.5	63.8±25.6
Post-PR	68.1±30.6	72.5±30.1	72.3±28.4
P	0.051	0.000	0.007
PI_{max} (cmH_2O)			
Pre-PR	43.6±21.6	41.8±17.7	40.3±19.2
Post-PR	54.1±31.8	51.2±23.8	50.7±22.9
P	0.314	0.001	0.000

Values are means±standard deviation.

Table 7 Activities of daily living scores: pre- and post-pulmonary rehabilitation (PR) by stage.

Parameters	Stages		
	II	III	IV
Velocity of motion			
Pre-PR	24.6±4.1	22.8±6.0	18.1±6.5
Post-PR	25.9±4.2	25.2±4.5	21.1±5.9
P	0.023	0.000	0.000
Shortness of breath			
Pre-PR	21.3±6.1	20.0±6.0	15.7±6.1
Post-PR	24.4±4.4	23.1±4.9	18.8±5.7
P	0.001	0.000	0.000

Values are means±standard deviation.

quality of life.[1,2] GOLD 2004 recommended PR for COPD patients from stage II ($FEV_1 < 80\%$).[6] Comprehensive PR is thought to be most effective when delivered as physiological training for 4–12 weeks, with strength training, respiratory muscle training, education, psychological and behavioral intervention, physiotherapy, relaxation exercises, and nutritional support.[11] Our comprehensive 4- to 8-week PR program was modeled on this concept. Berry et al.[3] showed that exercise training alone improved physical function in patients at all stages. The present study confirmed that patients with an $FEV_1 < 80\%$ (stages II, III, and IV) made gains in physical function with comprehensive PR. In the present study, the number of patients in each stage was very different: 21 in stage II, 79 in stage III, and 125 in stage IV. In Berry's study, the group with mild disease (corresponding to stage II in this study) included a large number of patients ($n = 99$) as compared with the moderate ($n = 36$) and severe ($n = 16$) groups.[3] The distribution of patients among the stages in our study was the opposite of Berry's study. Although an imbalance of patient numbers may result in significance at one stage and non-significance at another stage, Berry's study and our study showed a similar trend to improvement of pulmonary function. VC and %VC were significantly increased in all stages after PR although they did not mention about VC change. We do not have a clear explanation as to why the VC improved. We preliminary measured the expansion rate of thorax at inspiration and expiration in some patients. The ratio of expansion rates after and before PR was correlated with the VC increase (data not shown). This may be one of the reasons for the observed improvement.

In Berry's study, the average increase in 6 MWD after PR was 61.2, 72.7, and 34.2 m in mild, moderate, and severe disease, respectively. In the present study, the average increase in 6 MWD after PR was 48, 47, and 52 m in stages II, III and IV, respectively. Meta-analysis showed an average increase of 55.7 m in the 6MW test after PR, although they did not refer to stages.[1] The present study showed that 6 MWD was increased by approximately 50 m for the all staged patients. We acknowledge the need of a training session to avoid a learning effect biasing the results. However, all the patients did not always undergo the training session before PR. Of the 225 patients in this study, 21 were classified as having stage II COPD, 79 stage III, and 125 stage IV. The patients with stages II and III COPD tended to increase their 6 MWD to some extent after training session (by a several meters, at most). Some of the patients with stage IV were not willing to do the 6 MW test twice before PR because of breathlessness. Some did not walk as fast as possible without encouragement and their 6 MWD after training session decreased. Accordingly, we did not carry out a training session and accepted their first 6 MWD to unify the condition. The 6 MWD in patients in three stages of COPD was increased after PR up to approximately 50 m, which could not be explained by only the learning effect. However, we acknowledge the limits caused to the absence of a training session. In a future study, we should evaluate the real gain of 6 MWD by carrying out a training session. ΔSpO_2 was significantly increased (by an average of 1.4%) in patients with stage IV. PR improved the 6 MWD, but did not improve the ΔSpO_2. This result confirmed that ΔSpO_2 during walking was not correlated with distance.[12,13] Concerning respiratory muscle strength, Coppoolse et al.[14] reported that PI_{max} increased after PR although they did not refer to the severity of the disease. Our results showed that PE_{max} and PI_{max} were both significantly increased in stages III and IV. LVRS is considered the optional treatment for severe COPD[6] and we have previously reported that PR is the most important component of preparation prior to LVRS.[15] Improvement of respiratory muscle strength may contribute to the reduction of complications of LVRS. ADL were also improved in all stages after PR, which means that patients became more active with reduction of breathlessness. However, this study has a limitation about assessment of ADL. This ADL scale has not been validated in the English literature. It is not available internationally and is supported by only one published paper[8] although it is recommended from the Japanese Respiratory Society.[9] We should use a better known and accepted scale in a further study.

The present study confirmed that patients with COPD had benefited from PR regardless of disease severity. The effects included improvement in pulmonary function, arterial blood gas analysis, 6 MWD, respiratory muscle strength, and ADL, although there were some differences among the three stages. GOLD 2003 defined stage 0 (at risk) as normal spirometry with chronic symptoms and stage I (mild COPD) as $FEV_1/FVC < 70\%$ and $FEV_1 \geqslant 80\%$ predicted, in addition to stages II, III, and IV.[5] The usefulness of PR in stages 0 and I remains unclear. Because only two patients with stage I underwent PR during this study, we could not evaluate its effectiveness in stage I. The Nippon COPD Epidemiology study showed that the prevalence of airflow limitation ($FEV_1/FVC < 70\%$) was 10.9% in 2343 subjects aged 40 yr and that the severity of airflow limitation was: 56% stage I, 38% stage II, 5% stage III, and 1% stage IV.[16] Early intervention with comprehensive PR for early stages may be useful to increase patient awareness, reduce symptoms, and delay disease progression, and the indications for PR should be clarified.

Acknowledgements

We gratefully acknowledge the work of the specialist respiratory nurses, physical therapists and dieticians who supported this rehabilitation program.

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